arylalkoxy, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylamino, dialkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, arylcarbonylamino, aryloxycarbonylamino, azido, alkylthio, arylthio, perfluoroalkylthio, thiocyano, isothiocyano, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl or diarylamino-sulfonyl;

(b) separating and purifying the product of step (a);

(c) reacting the product of step (b) with a second monomer N^2, a dimer N^2-N^3 or a trimer N^2-N^3-N^4; and

(d) repeating steps (b) and (c) to produce an LPC-bound biopolymer having m monomers, where m is 3 to 100, wherein:

N^1, N^2, N^3...N^m are biopolymer monomers;

the dimers and trimers comprise the monomers; and

the protocol used in steps (c) and (d) to synthesize the biopolymer is the phosphoramidite protocol.

C 4 cont'd

REMARKS

Any fees that may be due in connection with filing this paper, or with this application or the parent application during their entire pendency, may be charged to Deposit Account No. 50-1213. If a Petition for Extension of Time is required, this paper is to be considered such petition.

Claims 6, 7, 9-11, 14-17, 20-22, 25, 26, 29, 31, 32, 39, 40, 45 and 47-49 are pending herein. Claims 6, 9-11, 39, 45 and 48 are amended herein. Basis for the amendments to the claims may be found in the claims as originally filed.

PROVISIONAL REJECTION OF CLAIMS 1-9 AND 27-49 FOR OBVIOUSNESS TYPE DOUBLE PATENTING

Claims 6, 7, 9-11, 14-17, 20-22, 25, 26, 29, 31, 39, 40, 45 and 47-49 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over the claims of copending U.S. application Serial No. 09/067,337. It is alleged in the Office Action that the claims in both the application are drawn to a liquid phase carrier (LPC), all being drawn from the same structural formulae and the substantial overlap in structure and intended modifications to the core of the structures represent subject matter covered by both applications claims.

Since obviousness-type double patenting cannot be assessed until there is allowable subject matter in one of the cases, applicant respectfully requests deferral of this issue until an indication that there is allowable subject matter in one of the cases. Until that time, the propriety of the rejection cannot be properly assessed. Upon review of the claims pending at the time, the need for a Terminal Disclaimer will be assessed, and, if needed, a Terminal Disclaimer will be provided.

REJECTION OF CLAIMS 6, 7, 9-11, 14-17, 20-22, 25, 26, 29, 31, 32, 45 AND 49 UNDER 35 U.S.C. §103(a)

Claims 6, 7, 9-11, 14-17, 20-22, 25, 26, 29, 31, 32, 45 and 49 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the teachings of U.S. Patent No. 5,198,540, to Köster *et al.* The Office Action alleges that the compounds of Köster *et al.* include LPCs possessing two to four points of attachment, which overlap with applicants optional number of points of attachment which include 3 to 6 points of attachment. The Office Action further alleges that the process claims of Köster *et. al* patent render applicants claimed methods *prima facie* obvious. It is alleged in the Office Action that the use of a known member of a class of materials (LPCs in the instant case) in a process to produce the expected product (oligonucleotide) or result

(biopolymeric synthesis) is not patentable if other members of the same class are known to be useful for the same purpose, even though the results are better than expected.

The Office Action notes that there are some differences between the compounds claimed and those of the prior art, specifically the instantly claimed LPCs have additional points of attachment. The Office Action concludes that the cited reference renders the instantly claimed LPCs *prima facie* obvious. Applicant respectfully traverses this rejection.

Summary of Arguments

Briefly, as discussed below, Applicant respectfully submits that the LPCs of instant formulae Ia, Ib, Ic, Id (where Y^2 = N), Ie and If, and of instant claim 45, are not taught or suggested by Köster *et al.* Nor does the cited reference teach or suggest modifications required to modify the LPCs taught therein to arrive at these LPCs of the instant claims.

Furthermore, as discussed below, and evidenced in the Declaration of Köster, of record herein, an LPC of instant formula Id, where Y^2 = CH, possesses properties not taught or suggested by the cited reference (improved yield when used in solution phase biopolymer synthesis when compared with the closest LPCs disclosed in the reference). Therefore, the LPCs of the instant claims are not obvious over the teachings of Köster *et al.*

Relevant Law

[I]n order to establish a *prima facie* case of obviousness, there must be evidence, preferably a teaching, suggestion, incentive or inference from the cited art or in the form of generally available knowledge that one of ordinary skill would have been led to modify the relevant teaching to arrive at what is claimed. *In re Papesch*, 315 F.2d 381, 391, 137 USPQ 43, 51 (CCPA 1963).

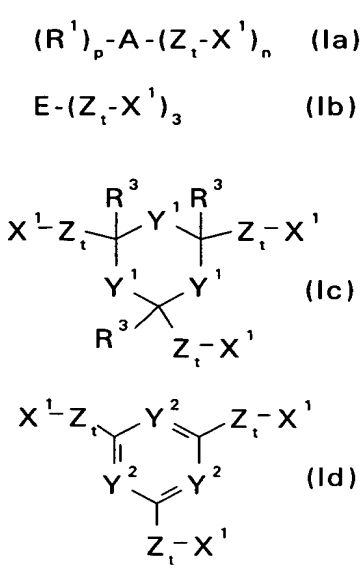
The prior art must provide a motivation whereby one of ordinary skill in the art would have been led to do that which the applicant has done. *Stratoflex Inc. v Aeroquip Corp.*, 713 F.2d 1530, 1535, 218 USPQ 871, 876 (Fed. Cir.

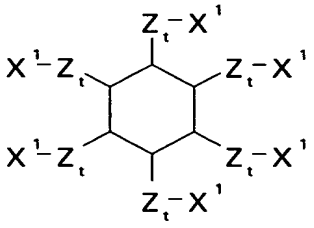
1983). In addition, the mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggests the desirability of the modification. *In re Fritch*, 23 USPQ 1783 (Fed. Cir. 1992).

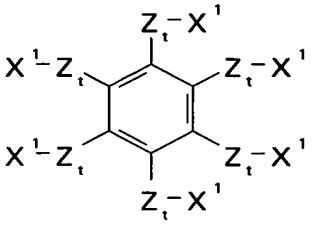
In addition, unexpected properties must always be considered in the determination of obviousness. A compound's structure and properties are inseparable so that unexpected properties are part of the subject matter as a whole. *In re Papesch*, 315 F.2d 381, 391, 137 USPQ 43, 51 (CCPA 1963).

The instant claims

Instant claim 6 is directed to a liquid phase carrier (LPC) of formulae (I):




(Ie)


(If)

where:

A is silicon;

E is nitrogen or P(O);

Y^1 is CH_2, NH, S or O;

Y^2 is selected from CH and N;

n is 3 or 4; and

the remaining variables are as defined therein.

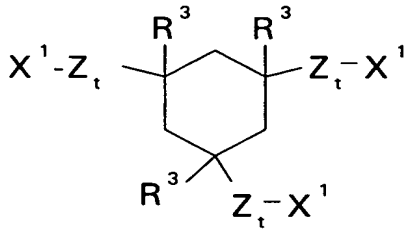
Claims 7 and 9 further define the variables in claim 6.

Claim 10 is directed to an LPC of claim 6 that has formulae (IIb):

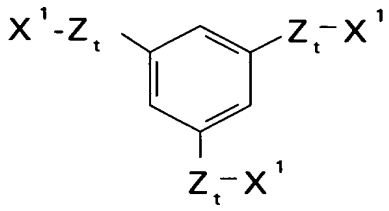
$N\text{-}(Z_t\text{-}X^1)_3$ (IIb)

where the variables are as defined therein. Claims 12-14 further define the variables in claim 10.

Claim 17 is directed to an LPC of claim 6 that has formulae (IIc) or (IId):



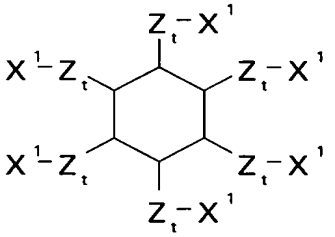
(IIc)



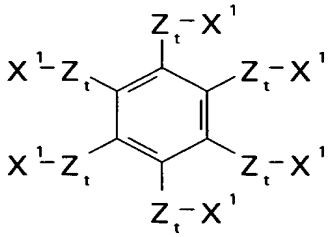
(IId)

where the variables are as defined therein. Claims 20 and 21 further define the variables in claim 17.

Claim 22 is directed to an LPC of claim 6 that has formulae (Ie) or (If):



(Ie)



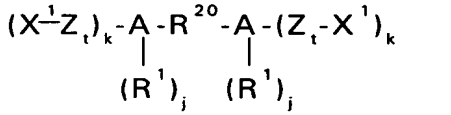
(If)

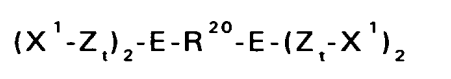
where the variables are as defined therein. Claims 25 and 26 further define the variables in claim 22.

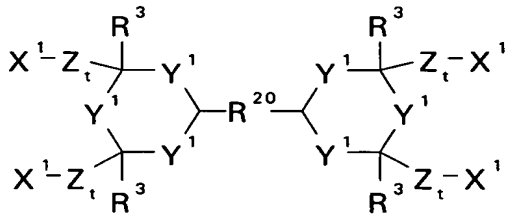
Claims 31 and 32 are directed to specific LPCs not disclosed in the cited reference.

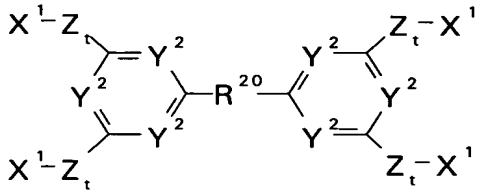
Claim 39 is directed to a method of solution phase biopolymer synthesis using an LPC of formulae (I). Claim 40 specifies certain LPCs for use in the method of claim 39. Claim 47 specifies certain monomers for use in the method of claim 39.

Claim 45 is directed to an LPC of formulae:









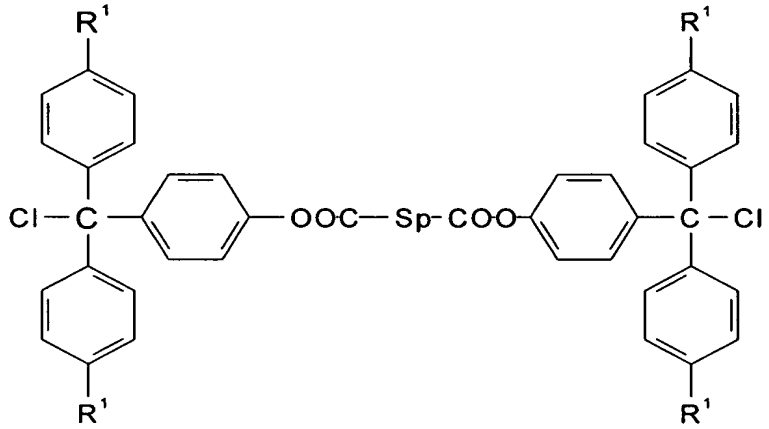
where the variables are as defined therein.

Claim 48 is directed to a method of solution phase biopolymer synthesis using an LPC of formulae (I) where the protocol used in the synthesis of the biopolymer is the phosphoramidite protocol.

Claim 49 is directed to the LPC of claim 6 coupled to a biopolymer.

Differences between the teachings of Köster *et al.* and the instant claims

U.S. Patent No. 5,198,540, to Köster *et al.*, teaches LPCs possessing two to four points of attachment of formula $Sp(X)_n$, where X is a reactive group which is compatible from the point of view of nucleotide chemistry, n is an integer from 2 to 4, and Sp is an optionally branched alkylene or polyalkylene group, an arylene or polyarylene group, a polyaralkylene group, a polyester, a polyamide, a polysiloxane, an optionally branched alkylenedioxy compound or optionally partially alkylated polyalkyleneoxy compound. The cited reference also teaches LPCs possessing two points of attachment having formulae:



X-OC-Sp-CO-X

In the instant application, the LPCs of claims 6, 7, 9-11, 14-17, 20-22, 25, 26, 29, 39-40, 47-49 have formulae I as described above, wherein a group that serves as the scaffold upon which synthesis of a plurality of oligomers is effected, has 3 to 6 points of attachments.

The LPCs of formula Ia

Applicant respectfully submits that the cited reference does not teach or suggest the LPCs of formula Ia (LPCs with 3 to 4 points of attachments) wherein A is silicon. Neither does it teach or suggest the structural

modifications required to modify the LPCs taught therein to arrive at the LPCs of instant formula Ia having a center of symmetry at a silicon atom.

Thus, one of ordinary skill in the art, given the teachings of Köster *et al.*, would not have motivated to do what applicant has done. Absent such motivation, the LPCs of instant formula Ia are not *prima facie* obvious over Köster *et al.*

The LPCs of formula Ib

Applicant respectfully submits that the cited reference does not teach or suggest the LPCs of formula Ib (LPCs with 3 points of attachments) wherein E is nitrogen or P(O). Neither does it teach or suggest the structural modifications to the LPCs taught therein to arrive at the LPCs of instant formula Ib.

Thus, one of ordinary skill in the art, given the teachings of Köster *et al.*, would not have motivated to do what applicant has done. Absent such motivation, the LPCs of instant formula Ib are not *prima facie* obvious over Köster *et al.*

The LPCs of formula Ic

Applicant respectfully submits that the cited reference does not teach or suggest the LPCs of formula Ic (LPCs with 3 points of attachments) having a center of symmetry at the center of a core cycloalkyl or heterocyclyl ring. Neither does it teach or suggest the structural modifications to the LPCs taught therein to arrive at the LPCs of instant formula Ic.

Thus, one of ordinary skill in the art, given the teachings of Köster *et al.*, would not have motivated to do what applicant has done. Absent such motivation, the LPCs of instant formula Ic are not *prima facie* obvious over Köster *et al.*

The LPCs of formula Id

Y^2 is Nitrogen

Applicant respectfully submits that the cited reference does not teach or suggest the LPCs of formula Id (LPCs with 3 points of attachments) having a

center of symmetry at the center of a core heteroaryl ring. Neither does it teach or suggest the structural modifications to the LPCs taught therein to arrive at the LPCs of instant formula Id, where $Y^2 = N$.

Thus, one of ordinary skill in the art, given the teachings of Köster *et al.*, would not have motivated to do what applicant has done. Absent such motivation, the LPCs of instant formula Id, where $Y^2 = N$, are not *prima facie* obvious over Köster *et al.*

The LPCs of formula Ie and If

Applicant respectfully submits that the cited reference does not teach or suggest the LPCs of formula Ie and formula If (LPCs with 6 points of attachments) having a center of symmetry at the center of a core cycloalkyl, heterocyclyl, aryl or heteroaryl ring, possessing 6 points of attachment neither does it teach or suggest the structural modifications to the LPCs taught therein to arrive at the LPCs of instant formulae Ie and If.

Thus, one of ordinary skill in the art, given the teachings of Köster *et al.*, would not have motivated to do what applicant has done. Absent such motivation, the LPCs of instant formulae Ie and If are not *prima facie* obvious over Köster *et al.*

The cited reference does not teach or suggest LPCs of dependent claims with formula II (b-d) possessing 3 points of attachment, as required by instant claims 10, 14-17, 20 and 21. Nor does the cited reference teach or suggest the LPCs of formulae (Ie) or (If) possessing 6 points of attachment, as required by instant claims 22, 25 and 26. The reference also does not teach or suggest the specific LPCs claimed in instant claims 31 and 32.

The LPCs of claim 45

The LPCs of instant claim 45 possess 4, 5 or 6 points of attachment and are composed of two of the groups of formulae (I) linked together by R^{20}, wherein R^{20} is alkylene, alkenylene, alkynylene, arylene or heteroarylene. The cited art does not teach or suggest such LPCs. Neither does it teach or suggest

the structural modifications to the LPCs taught therein to arrive at the LPCs of instant claim 45.

Thus, one of ordinary skill in the art, given the teachings of Köster *et al.*, would not have motivated to do what applicant has done. Absent such motivation, the LPCs of instant claim 45 are not *prima facie* obvious over Köster *et al.*

Methods of using LPCs

Furthermore, the cited reference does not teach or suggest methods of using LPCs of instant formulae Ia-Id (where $Y^2=N$) and Ie-If, possessing 3 to 6 points of attachment in solution phase biopolymer synthesis, as claimed in instant claims 39 and 47-48, because as discussed above, it does not teach or suggest the LPCs of instant formulae Ia-Id (where $Y^2=N$) and Ie-If. Neither does it teach or suggest the structural modifications required to modify the LPCs disclosed therein to arrive at the instant LPCs, having a center of symmetry at a single atom or at the center of a core cycloalkyl, heterocyclyl, aryl or heteroaryl ring, possessing 3 to 6 points of attachment, for use in the instant methods. Nor does the cited reference teach or suggest methods of solution phase biopolymer synthesis using the specific LPCs of claim 40, because as discussed above, it does not teach or suggest the specific LPCs.

Absent such teaching or suggestion, one of ordinary skill in the art would not have been motivated to do what applicant has done. Applicant respectfully submits that one of ordinary skill in the art, given the teachings of U.S. Patent No. 5,198,540, would not have been motivated to prepare the LPCs of instant formulae Ia-Id (where $Y^2=N$) and Ie-If, for use in solution phase biopolymer synthesis. Absent such motivation, the instant claims are not *prima facie* obvious over the teachings of the cited reference.

Therefore, the Office Action fails to establish a *prima facie* case of obviousness for the LPCs of instant formulae Ia-Id (where $Y^2 = N$) and Ie-If, and claim 45.

In order to establish a *prima facie* case of obviousness, there must be some teaching or suggestion in the cited art that would motivate one of ordinary skill in the art to do what applicant has done. It is respectfully submitted that no such motivation exists in U.S. Patent No. 5,198,540. The cited reference teaches a generic class of LPCs possessing 2 to 4 points of attachment. The cited reference neither teaches or suggests the instantly claimed classes of LPCs of formulae Ia-Id (where $Y^2 = N$) and Ie-If, and of instant claim 45, possessing 3 to 6 points of attachment nor does it teach or suggest the structural modifications required to modify the LPCs taught therein to arrive at the LPCs of formulae Ia-Id (where $Y^2 = N$) and Ie-If. The cited reference does not teach or suggest LPCs of dependent claims with formula II (b-d) possessing 3 points of attachment, as required by instant claims 10, 14-17, 20 and 21. Nor does it teach or suggest the LPCs of instant formulae (Ie) or (If) possessing 6 points of attachment, as required by instant claims 22, 25 and 26. The reference also does not teach or suggest the specific LPCs claimed in instant claims 31 and 32. Nor does the reference teach or suggest the LPCs of instant claim 45 that possess 4, 5 or 6 points of attachment as discussed above.

Since the cited reference does not teach or suggest LPCs of the instant formulae Ia-Id (where $Y^2 = N$) and Ie-If, it cannot teach or suggest methods of solution phase biopolymer synthesis using the LPCs of the instant formulae Ia-Id (where $Y^2 = N$) and Ie-If, nor can it teach or suggest the LPCs of the instant formulae Ia-Id (where $Y^2 = N$) and Ie-If, coupled to a biopolymer. Therefore, the Office Action has failed to set forth a *prima facie* case of obviousness for these LPCs of the instant claims.

The LPCs of instant formula Id, where $Y^2 = CH$, possesses properties not taught or suggested by the cited reference

Applicant has provided a Declaration of Köster demonstrating the increase in the yield of solution phase biopolymer synthesis achieved with the LPCs of instant formula Id, where Y^2 is CH, versus the results provided in the cited reference for the yield of solution phase biopolymer synthesis using the divalent LPCs taught therein. Specifically, the use of an LPC of the instant formula Id, where Y^2 is CH, provides a 10-mer oligonucleotide in an overall yield of 33%, as compared to overall yields of a 5-mer, 6-mer and a 7-mer of 14%, 8% and 5%, respectively, using the LPC of the cited reference. The structural modifications required to achieve this increase in yield are not taught or suggested by the cited reference.

As discussed above, the Declaration of Köster shows that an LPC with formula Id, where Y^2 is CH, having a center of symmetry at the center of a core aryl ring possesses properties not taught or suggested by U.S. Patent No. 5,198,540. The increase in yield obtained using this multivalent LPC of the instant application is neither taught nor suggested by the cited reference, which teaches use of divalent LPCs. Nor does the cited reference teach or suggest the structural modifications required to achieve the above-noted increase in solution phase biopolymer synthesis yield. Therefore, the instant claims are not obvious over the teachings of U.S. Patent No. 5,198,540.

Rebuttal to the specific arguments in the Office Action

1. It is alleged in the Office Action that the compounds of Köster *et al.* include LPCs possessing 2 to 4 points of attachments, which overlaps with applicant's optional number of points of attachment which include 3 to 6 points of attachment and that the overlap is undeniable.

The applicant respectfully submits that as discussed above, the instantly claimed LPCs of formulae Ia-Id (where $Y^2 = N$) and Ie-If, and of claim 45 are structurally different than the LPCs in Köster *et al.* reference, therefore there is

no overlap between these formulae and the teachings of Köster *et al.* The instantly claimed LPCs of formulae Ia-Id (where $Y^2 = N$) and Ie-If, and of claim 45, and the methods of biopolymer synthesis using the LPCs, having a center of symmetry at a single atom or at the center of a core cycloalkyl, heterocyclyl, aryl or heteroaryl ring, possessing 3 to 6 points of attachment, are not taught or suggested in the cited reference.

2. The Office Action alleges that it would have been obvious to one having ordinary skill in the art at the time of the invention was made to formulate LPCs with multiple points of attachment and variable structure, because the prior art teaches such LPCs.

The applicant respectfully submits that as discussed above, the prior art **does not** teach or suggest the LPCs of instant application having formulae Ia-Id (where $Y^2 = N$) and Ie-If, and of claim 45. Neither does it teach or suggest the structural modifications required to modify the LPCs taught therein needed to arrive at the LPCs of the instant claims. Therefore, the cited reference does not provide any motivation to prepare the LPCs of instant formulae Ia-Id (where $Y^2 = N$) and Ie-If for use in solution phase biopolymer synthesis. Absent such a motivation, LPCs of instant formulae Ia-Id (where $Y^2 = N$) and Ie-If are not *prima facia* obvious over the teachings of the cited art.

The Declaration of Köster

The Office Action alleges that the Declaration does not show data comparing the yields of oligonucleotide synthesis using LPCs of the instant claims. The Office Action alleges that this is misrepresentation of what the Declaration actually provides, and that the Declaration actually provides data comparing LPCs of the prior art with two points of attachment with a single representation of an LPC of the instant claims.

Applicant respectfully submits that there was an inadvertent typographical error in the recitation:

the Declaration provides data comparing the yields of oligonucleotide synthesis using LPCs of the instant claims.

There was no intent to misrepresent the data. The Declaration was provided to compare the yield of oligonucleotide synthesis using a representative example of an LPC of instant formula Id, where $Y^2 = CH$, with the closest LPC disclosed in the reference.

The Office Action further alleges that the Declaration provides a comparison of yields, but the Examiner can not determine whether the reaction conditions for the oligonucleotide synthesis using the LPCs of the prior art and the singular example provided in the Declaration as representative of the LPCs instantly claimed were indeed used in methodological procedures the skilled artisan would consider correlative and sufficient for a side-by-side analysis. The Office Action alleges that no data or reaction conditions showing a true side by side comparison is seen in the Declaration of April 16, 2002.

The applicant respectfully submits that the Declaration describes the reaction conditions for oligonucleotide synthesis using a representative LPC with three points of attachments (e.g., see page 7-8) and Köster *et al.* patent 5,198,540 describes the reaction conditions for the oligonucleotide synthesis using the LPCs with 2 to 4 points of attachment, claimed therein (e.g., see column 8). Therefore, a skilled artisan would be able to determine if the reaction conditions used in the methodological procedures were correlative and sufficient for a side-by-side analysis.

The Office Action urges that the applicant is directed to their admission that the prior art contemplates LPCs with 2 to 4 points of attachments which overlap with the points of attachment for the LPC set forth in the Declaration. The Office Action alleges that applicant admits on page 7, lines 7-8 of the Declaration, that one skilled in this art would be motivated from 5,198,540

patent of record to use an LPC with three points of attachment, as well as four points of attachment, as instantly claimed.

The applicant strongly disagrees. It is respectfully submitted that page 7, lines 7-8, of the Declaration gives NMR data for the LPC with 3 points of attachment. The above quoted lines are recited below:

> (C5'), 74.68 (C3'), 83.60/84.47 (C1'/C4'), 109.64 (C5, Base), 128.48 (CH_{Ar}), 134.78 (C_{Ar}), 135.74 (C6, Base), 150.39 (C2, Base), 163.57 (C4, Base),

Applicant does not admit anywhere in the Declaration, or in the previous response that one of ordinary skill in this art would be motivated, given the teachings of U.S. Patent 5,198,540, to use an LPC with three points of attachment, as well as four points of attachment, as instantly claimed. The instantly claimed LPCs with 3 to 6 points of attachment are structurally different than the LPCs of the cited reference. The cited reference does not teach or suggest instant LPCs of formulae Ia-Id (where $Y^2 = N$) and Ie-If. Neither does it teach or suggests the structural modifications to the LPCs taught therein needed to arrive at the LPCs of the instant claims. Furthermore, the cited reference does not provide any motivation to prepare the LPCs of instant of formulae Ia-Id (where $Y^2 = N$) and Ie-If, for use in solution phase biopolymer synthesis. The allegation that applicant admits that one of ordinay skill in this art would be motivated from the teachings of U.S.Patent 5,198,540, to use the LPC of instant formulae Ia-Id (where $Y^2 = N$) and Ie-If, as instantly claimed, is improper.

The Office Action further urges that a better example for comparison would have been LPCs as instantly claimed which have 3 and 4 points of attachment correlative to those of the prior art with overlapping number of points of attachment, since the prior art appears to indicate that such compounds would be expected to succeed as LPCs in oligonucleotide synthesis.

The Office Action further alleges that the overlap is clear and relevant to the teachings which render applicants compounds *prima facie* obvious.

Applicant respectfully submits that Köster *et al.*, does not provide data on yields of oligonucleotide synthesis using LPCs with 3 or 4 points of attachment. It provides data only for an LPC with 2 points of attachment. The Declaration provides data for comparison of yields of oligonucleotide synthesis using a representative example of instantly claimed LPCs of formula Id, where $Y^2 = CH$, with the closest disclosed LPC in the prior art. Nothing further is, or should be required.

Applicant respectfully requests reconsideration and withdrawal of this rejection.

* * *

In view of the above, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	KÖSTER *et al.*
Serial No.:	09/484,484
Confirmation No.:	9747
Filed:	January 18, 2000
For:	*SOLUTION PHASE BIOPOLYMER SYNTHESIS*
Art Unit:	1623
Examiner:	Wilson, J.

ATTACHMENTS TO RESPONSE TO OFFICE ACTION

The following attachment is provided:

(1) Marked up claims 6, 9-11, 39, 45 and 48 in accord with 37 CFR §1.121.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: KÖSTER *et al.*

Serial No.: 09/484,484

Confirmation No.: 9747

Filed: January 18, 2000

For: *SOLUTION PHASE BIOPOLYMER SYNTHESIS*

Art Unit: 1623

Examiner: Wilson, J.

MARKED UP CLAIMS (37 CFR §1.121)

Please amend claims 6, 9, 10, 11, 39, 45 and 48 as follows:

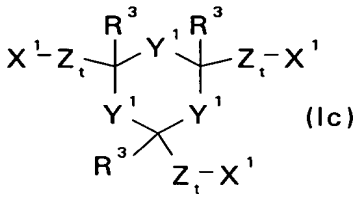
IN THE CLAIMS:

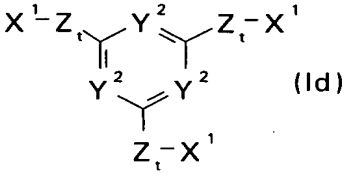
Please replace claims 6, 9, 10, 11, 39, 45 and 48 with the following claims:

6. (Amended Twice) A liquid phase carrier (LPC) that has formulae (I):

$(R^1)_p$-A-$(Z_t$-$X^1)_n$ (Ia)

E-$(Z_t$-$X^1)_3$ (Ib)


(Ic)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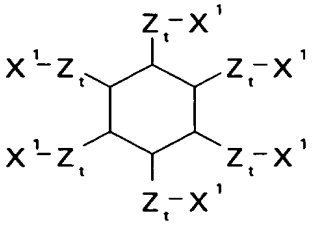
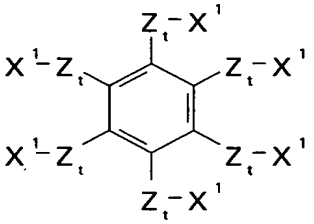

(Ie)


(If)

wherein: A is [carbon or] silicon; E is nitrogen or P(O); R^1 and R^3 are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; p is 0 or 1; Z is any combination of 1-12 units

selected from 1,4-phenylene and methylene units, which units may be combined in any order, with the proviso that if the LPC is of formula (Ia) or (Ib), then Z contains at least two phenylene or methylene units; t is 1; X^1 is OH, SH, NH_2, COR^5 or $COOR^4$ where R^4 is selected from hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl and heterocyclylalkyl, and R^5 is halide, heteroaryl or pseudohalide; n is 3 or 4; Y^1 is CH_2, NH, S or O; Y^2 is selected from CH and N; R^1, R^3, X^1, Y^1, Y^2 and Z are unsubstituted or substituted with one or more substituents each independently selected from Q; and Q is halogen, hydroxy, nitrile, nitro, formyl, mercapto, carboxy, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, arylalkoxy, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylamino, dialkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, arylcarbonylamino, aryloxycarbonylamino, azido, alkylthio, arylthio, perfluoroalkylthio, thiocyano, isothiocyano, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl or diarylaminosulfonyl.

9. (Amended) The LPC of claim 6, wherein: [A is carbon and] E is nitrogen.

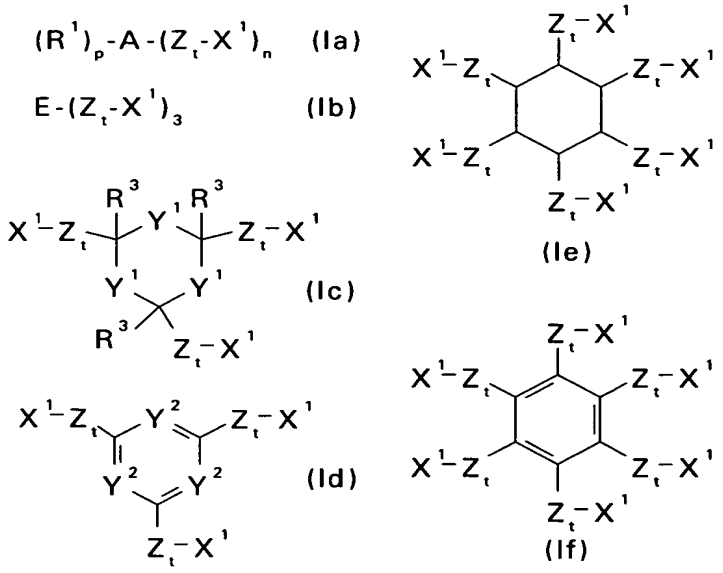
10. (Amended) The LPC of claim 6, wherein the LPC has [formulae (IIa) or] <u>formula</u> (IIb):

$N\text{-}(Z_t\text{-}X^1)_3$ (IIb).

11. (Amended) The LPC of claim [10] <u>6</u>, wherein p is 0 and n is 4.

39. (Amended) A method of solution phase biopolymer synthesis, comprising the steps of:

(a) reacting an LPC with a first monomer N^1; wherein the LPC has formulae (I):



wherein: A is [carbon or] silicon; E is nitrogen or P(O); R^1 and R^3 are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; p is 0 or 1; Z is any combination of 0-12 units selected from 1,4-phenylene and methylene, which units may be combined in any order; t is 0 or 1; X^1 is OH, SH, NH_2, COR^5 or $COOR^4$, where R^4 is selected from hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl and heterocyclylalkyl; and R^5 is halide, heteroaryl or pseudohalide; n is 3 or 4; Y^1 is CH_2, NH, S or O; Y^2 is selected from CH and N; R^1, R^3, X^1, Y^1, Y^2 and Z are unsubstituted or substituted with one or more substituents each independently selected from Q; and Q is halogen, hydroxy, nitrile, nitro, formyl, mercapto, carboxy, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkylidene,

arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, arylalkoxy, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylamino, dialkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, arylcarbonylamino, aryloxycarbonylamino, azido, alkylthio, arylthio, perfluoroalkylthio, thiocyano, isothiocyano, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl or diarylaminosulfonyl;

(b) separating and purifying the product of step (a);

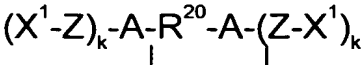
(c) reacting the product of step (b) with a second monomer N^2, a dimer N^2-N^3 or a trimer N^2-N^3-N^4; and

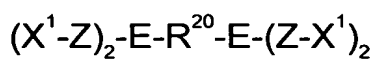
(d) repeating steps (b) and (c) to produce an LPC-bound biopolymer having m monomers, where m is 3 to 100, wherein:

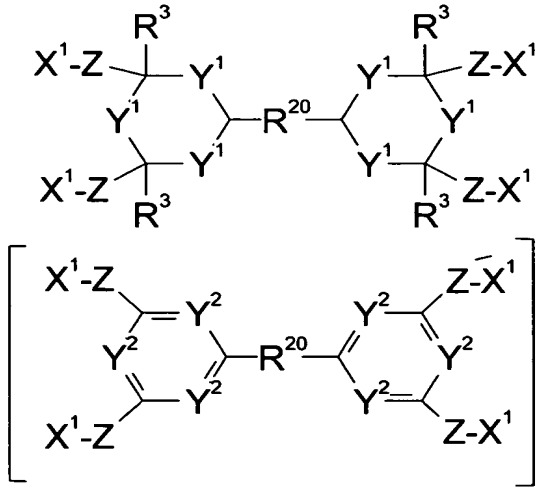
N^1, N^2, N^3...N^m are biopolymer monomers; and

the dimers and trimers comprise the monomers.

45. (Amended) A liquid phase carrier (LPC) that has formulae:





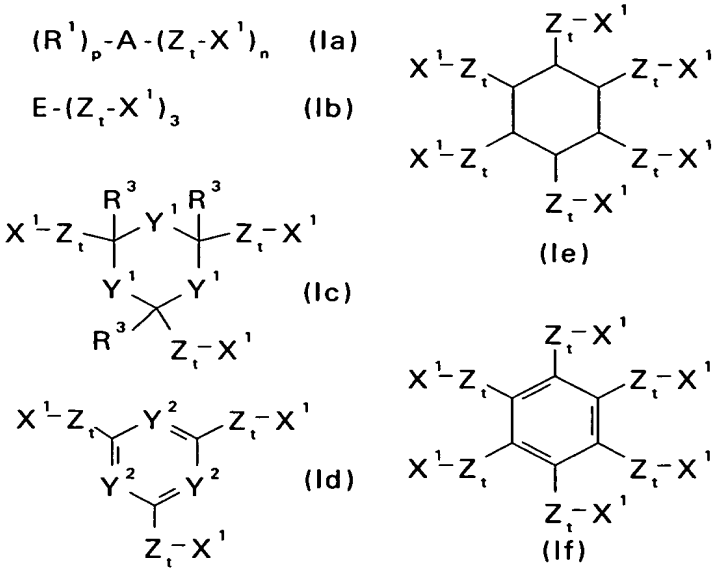


wherein: A is silicon; E is nitrogen or P(O); R^1 and R^3 are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; Z is any combination of 1-12 units selected from 1,4-phenylene and methylene, which units may be combined in any order, with the proviso that if the LPC is of formula (Ia) or (Ib), then Z contains at least two phenylene or methylene units; t is 0 or 1; X^1 is OH, SH, NH_2, COR^5 or $COOR^4$, where R^4 is selected from hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl and heterocyclylalkyl; and R^5 is halide, heteroaryl or pseudohalide; Y^1 is CH_2, NH, S or O; Y^2 is selected from CH and N; R^1, R^3, X^1, Y^1, Y^2 and Z are unsubstituted or substituted with one or more substituents each independently selected from Q; and Q is halogen, hydroxy, nitrile, nitro,

formyl, mercapto, carboxy, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, arylalkoxy, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylamino, dialkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, arylcarbonylamino, aryloxycarbonylamino, azido, alkylthio, arylthio, perfluoroalkylthio, thiocyano, isothiocyano, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl or diarylaminosulfonyl; R^{20} is alkylene, alkenylene, alkynylene, arylene or heteroarylene; k is 2 or 3; and j is 0 or 1.

48. (Amended) A method of solution phase biopolymer synthesis, comprising the steps of:

(a) reacting an LPC with a first monomer N^1; wherein the LPC has formulae (I):



wherein: A is [carbon or] silicon; E is nitrogen or P(O); R^1 and R^3 are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; p is 0 or 1; Z is any combination of 0-12 units selected from 1,2-, 1,3- or 1,4-phenylene and alkylene, which units may be combined in any order; t is 0 or 1; X^1 is OH, SH, NH_2, COR^5 or $COOR^4$, where R^4 is selected from hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl and heterocyclylalkyl; and R^5 is halide, heteroaryl or pseudohalide; n is 3 or 4; Y^1 is CH_2, NH, S or O; Y^2 is selected from CH and N; R^1, R^3, X^1, Y^1, Y^2 and Z are unsubstituted or substituted with one or more substituents each independently selected from Q; and Q is halogen, hydroxy, nitrile, nitro, formyl, mercapto, carboxy, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, perfluoroalkoxy, alkenyloxy, alkynyloxy,

arylalkoxy, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylamino, dialkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, arylcarbonylamino, aryloxycarbonylamino, azido, alkylthio, arylthio, perfluoroalkylthio, thiocyano, isothiocyano, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl or diarylamino-sulfonyl;

(b) separating and purifying the product of step (a);

(c) reacting the product of step (b) with a second monomer N^2, a dimer N^2-N^3 or a trimer N^2-N^3-N^4; and

(d) repeating steps (b) and (c) to produce an LPC-bound biopolymer having m monomers, where m is 3 to 100, wherein:

N^1, N^2, N^3...N^m are biopolymer monomers;

the dimers and trimers comprise the monomers; and

the protocol used in steps (c) and (d) to synthesize the biopolymer is the phosphoramidite protocol.